

WEST Search History

DATE: Monday, January 06, 2003

Set Name Query
side by side

Hit Count Set Name
result set

DB=USPT,PGPB,EPAB,DWPI; PLUR=YES; OP=ADJ

L1	disrupted-in-schizophrenia or DISC1	17	L1
L2	disrupted-in-schizophrenia	2	L2
L3	devon-rs.in. or adnerson-s\$.in. or burgess-PS.in. or Teague-PW.in. or kipari tM.in or semple-CS.in. or millar JK.in. or muir -wj.in.	91	L3
L4	l3 and schizophrenia	0	L4
L5	porteous-d\$.in. or millar-K\$.in. or Blachwood-D\$.in.	76	L5
L6	L5 and l2	0	L6
L7	L5 and schizophrenia	1	L7

DB=USPT,DWPI; PLUR=YES; OP=ADJ

L8	disrupted-in-schizophrenia or disrupted in schizophrenia or DIS1	91	L8
L9	disrupted-in-schizophrenia or disrupted in schizophrenia or (DIS1 and schizophrenia)	1	L9
L10	L9	1	L10

END OF SEARCH HISTORY

Identification of polymorphisms within **Disrupted**
in **Schizophrenia 1** and **Disrupted** in
Schizophrenia 2, and an investigation of their
association with schizophrenia and bipolar affective
disorder.

AUTHOR: Devon R S; Anderson S; Teague P W; Burgess P; Kipari T M;
Semple C A; Millar J K; Muir W J; Murray V; Pelosi A J;
Blackwood D H; Porteous D J

CORPORATE SOURCE: Medical Genetics Section, University of Edinburgh,
Molecular Medicine Centre, Western General Hospital, UK..
rebecca@cmmmt.ubc.ca

SOURCE: PSYCHIATRIC GENETICS, (2001 Jun) 11 (2) 71-8.
Journal code: 9106748. ISSN: 0955-8829.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200203

ENTRY DATE: Entered STN: 20010830

Last Updated on STN: 20020308

Entered Medline: 20020307

AB We have undertaken a search for polymorphic sequence variation within
Disrupted in **Schizophrenia 1** and **Disrupted** in
Schizophrenia 2 (**DISC1** and **DISC2**), which are both novel
genes that span a translocation breakpoint strongly associated with
schizophrenia and related psychoses in a large Scottish family. A scan of
the coding sequence, intron/exon boundaries, and part of the 5' and 3'
untranslated regions of **DISC1**, plus 2.7 kb at the 3' end of
DISC2, has revealed a novel microsatellite and 15 novel single nucleotide
polymorphisms (SNPs). We have tracked the inheritance of four of the SNPs
through multiply affected families, and carried out case-control
association studies using the microsatellite and four common SNPs on
populations of patients with schizophrenia or bipolar affective disorder
versus normal control subjects. Neither co-segregation with disease

status

nor significant association was detected; however, we could not detect
linkage disequilibrium between all these markers in the control
population, arguing that an even greater density of informative markers

is

required to test rigorously for association in this genomic region.

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population, arguing that an even greater density of informative markers
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required to test rigorously for association in this genomic region.

Chromosomal location and genomic structure of the human
translin-associated factor X gene (TRAX; TSNAX) revealed
by

intergenic splicing to **DISC1**, a gene disrupted by
a translocation segregating with schizophrenia.
AUTHOR: Millar J K; Christie S; Semple C A; Porteous D J
CORPORATE SOURCE: Department of Medical Sciences, The University of
Edinburgh, Scotland, United Kingdom..
Kirsty.Millar@ed.ac.uk
SOURCE: GENOMICS, (2000 Jul 1) 67 (1) 69-77.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF222988; GENBANK-AF230314; GENBANK-AF230315;
GENBANK-AF230316; GENBANK-AF230317
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111

AB Two candidate genes, **DISC1** and **DISC2** on chromosome 1, are
disrupted by a translocation that segregates with major psychiatric
illness. Several **DISC1** transcripts contain TRAX (HGMW-approved
symbol TSNAX) sequence at the 5' end. These transcripts initiate at the

5' end of TRAX and terminate at the final exon of **DISC1**. Five
species of transcript resulting from intergenic splicing have been
identified; one encodes a novel TRAX/**DISC1** fusion protein. The
remaining four transcripts are bicistronic and encode a series of novel
truncated isoforms of TRAX and **DISC1**. Demonstration that the
various TRAX/**DISC1** transcripts are translated awaits further
experimentation. As a consequence of the observation of intergenic
splicing, the human TRAX gene has been mapped at least 35 kb proximal to
DISC1 and within approximately 150-250 kb of the translocation
breakpoint at 1q42.1. The TRAX gene consists of six exons with a putative
CpG island at the 5' end. Four major transcripts are produced from this
gene, of which the smallest, at 2.7 kb, had previously been identified.

PREV200100547661

TITLE: Evaluation of DISC-1 expression in human brains.
AUTHOR(S): Ozeki, Y. (1); Fujii, K. (1); Kamiya, A. (1); Otsuki, H. (1); Luo, X.; Yamada, N. (1); Margolis, R. L.; Ohkawa, M. (1); Snyder, S. H.; Ross, C. A.; Sawa, A.
CORPORATE SOURCE: (1) Psychiatry, Shiga Univ Med Sci, Otsu Japan
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 1493. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB DISC-1 (**Disrupted-In-Schizophrenia**) is a transcript whose open reading frame is disrupted by a balanced chromosomal translocation in a large Scottish family. The chromosomal translocation is highly associated with major mental illnesses in the family, suggesting that DISC-1 may confer vulnerability to major mental illnesses, especially schizophrenia. In our preliminary in situ hybridization experiments in rat, we found high expression of DISC-1 messenger RNA in olfactory bulb, moderate expression of DISC-1 in hippocampus and cortex, and little in cerebellum. This could be consistent with a function in olfaction, limbic functioning, cognition, and memory, processes thought to be involved in schizophrenia. To evaluate protein expression of DISC-1, we have developed an antibody against DISC-1. We generated a recombinant protein of 254 amino acids in C terminal end of DISC-1 conjugated with GST in E. coli. We purified the recombinant protein from the extract of E. coli, and used the antigen to produce antisera against DISC-1 in rabbits. After obtaining the antisera, we have obtained a pure antibody against DISC-1 through immuno-affinity columns. Using the antibody, we have confirmed the existence of DISC-1 at protein level, which is enriched in olfactory bulb and hippocampus. We are now collecting brains with schizophrenia and normal control subjects, to compare DISC-1 expression between patients and controls.

Disruption of two novel genes by a translocation
co-segregating with schizophrenia.

AUTHOR: Millar J K; Wilson-Annan J C; Anderson S; Christie S;
Taylor M S; Semple C A; Devon R S; Clair D M; Muir W J;
Blackwood D H; Porteous D J

CORPORATE SOURCE: Medical Genetics Section, Department of Medical Sciences,
The University of Edinburgh, Molecular Medicine Centre and
MRC Human Genetics Unit, both at Western General Hospital,
Crewe Road, Edinburgh EH4 2XU, UK.. kirsty.millar@ed.ac.uk

SOURCE: HUMAN MOLECULAR GENETICS, (2000 May 22) 9 (9) 1415-23.
Journal code: 9208958. ISSN: 0964-6906.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200008

ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000829

AB A balanced (1;11)(q42.1;q14.3) translocation segregates with
schizophrenia

and related psychiatric disorders in a large Scottish family (maximum LOD
= 6.0). We hypothesize that the translocation is the causative event and
that it directly disrupts gene function. We previously reported a dearth
of genes in the breakpoint region of chromosome 11 and it is therefore
unlikely that the expression of any genes on this chromosome has been
affected by the translocation. By contrast, the corresponding region on
chromosome 1 is gene dense and, not one, but two novel genes are directly
disrupted by the translocation. These genes have been provisionally named
Disrupted-In-Schizophrenia 1 and 2 (**DISC1** and
DISC2). **DISC1** encodes a large protein with no significant
sequence homology to other known proteins. It is predicted to consist of

a globular N-terminal domain(s) and helical C-terminal domain which has the
potential to form a coiled-coil by interaction with another, as yet,
unidentified protein(s). Similar structures are thought to be present in

a variety of unrelated proteins that are known to function in the nervous
system. The putative structure of the protein encoded by **DISC1**
is therefore compatible with a role in the nervous system. DISC2
apparently specifies a non-coding RNA molecule that is antisense to
DISC1, an arrangement that has been observed at other loci where
it is thought that the antisense RNA is involved in regulating expression
of the sense gene. Altogether, these observations indicate that
DISC1 and DISC2 should be considered formal candidate genes for
susceptibility to psychiatric illness.

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ACCESSION NUMBER: 2001-12456 BIOTECHDS

TITLE: Novel isolated polynucleotide which surrounds a breakpoint
on

chromosome 1 involved in a balanced t(1;11) (q42.1;q14.3)
translocation, and its encoded proteins, useful as

medicament

for treating psychiatric disorders;
involving vector-mediated gene transfer for expression in
host cell

AUTHOR: Porteous D; Millar K; Blackwood D

PATENT ASSIGNEE: Akzo-Nobel; Med.Res.Counc.; Univ.Edinburgh

LOCATION: Velperweg, The Netherlands; London, UK; Edinburgh, UK.

PATENT INFO: WO 2001040301 7 Jun 2001

APPLICATION INFO: WO 2000-EP11915 28 Nov 2000

PRIORITY INFO: EP 1999-309667 1 Dec 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-374796 [39]

AN 2001-12456 BIOTECHDS

AB A substantially pure polynucleotide (I), encoding a fully defined
disrupted in **schizophrenia** (DIS)1 amino acid sequence
of 854 or 832 amino acids, or their isoforms, is claimed. Also claimed
are: a recombinant expression vector (II) comprising (I) or its
fragments; a protein (III) having the disclosed sequence or its

isoforms;

cell line transformed with (I) encoding (III); cell line transformed

with

(I) or its fragments or transformed with (II); use of a polynucleotide
hybridizable to the DIS1 gene in the in vitro diagnosis of a psychiatric
disorder; antibodies against (III); and a pair of oligonucleotide
primers. (III) encoded by (I), or its fragments and the cell line is
useful for in vitro diagnosis of a psychiatric disorder. (I) or its
fragments or (II) is useful in screening assay for identifying new

drugs.

(III), its analogs or fragments, and cell lines are also useful for
identifying new drugs for treating psychiatric disorders. (III) is
useful as a therapeutic agent in that they may substitute the gene
product in the individuals with aberrant expression of DIS1 gene.

(51pp)

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